REMARKS

This Amendment After Final is in response to the Final Official Action mailed November 3, 1995 wherein claims 1, 2, 9 and 12-14 were rejected under 35 U.S.C. §112, ¶1; claims 1-6, 8, 13-16 and 19 were rejected under 35 U.S.C. §103 over GALATIK et al. (Czechoslovak 264,719); claims 7 and 17 were rejected under 35 U.S.C. §103 over GALATIK et al., Balazs (U.S. 4,141,973) and Shimizu et al. (U.S. 4,024,073); Claims 9-12 were rejected under 35 U.S.C. §103 over GALATIK and Applicant's disclosure at page 10, lines 15-27. The rejection of claims 1-6, 8 and 13-16 under 35 U.S.C. §102(b) as being anticipated by GALATIK et al. (Czechoslovakian Patent No. 264,719) has been withdrawn by the Examiner.

Applicants have now canceled claims 13-14 and 16, and have amended claims 1, 2, 5, 17 and 19. Claims 1-12, 15, 17 and 19 remain in the case and are believed to be allowable as amended. Reconsideration and allowance of claims 1-12, 15, 17 and 19 is respectfully requested. In the alternative, Applicants request that this amendment be entered as it places the claims in better condition for consideration on appeal.

In that regard, the undersigned attorney Leoniede Brennan spoke with Examiner White on January 23, 1996 who agreed to the scheduling of an interview (following the filing of the instant Amendment After Final and Notice of Appeal) most likely during the second week of March, 1996.

§112 Issues

Claims 1, 2, 9 and 12-14 have been rejected under 35 U.S.C. §112, ¶1 upon the Examiner's contention that the disclosure is "enabling only for claims limited [to] hyaluronic acid having a molecular weight range of 550,000 to 8,000,000 (see page 6, lines 26-30 of the specification)", and that "[t]here appears to be no reference to other polysaccharides having this molecular weight range". The foregoing amendments to claims 1-2, and the cancellation of claims 13-14 limits the claims to adhesion preventatives derived from hyaluronic acid or an alkali or alkaline earth metal salt thereof. These amendments are believed to remove the basis of this rejection. Such amendment is not, however, an admission of or acceptance of the grounds for the §112 rejection and Applicant reserves the right to further prosecute in a continuing application claims directed to the canceled subject matter.

In view of the limitation of the subject matter of the pending claims to adhesion preventatives derived from hyaluronic acid or a salt thereof, withdrawal of the §112, ¶ 1 rejection is respectfully requested.

Applicant has also amended the claims to remove ambiguities observed in preparing this response. Specifically:

Claim 2 has also been amended to clarify that the alkali and alkali salts are alternatives, see page 5, lines 4-6;

Claim 5 has been amended to correspond to the trivalent antecedent of claim 1;

Claim 16 has been canceled as redundant of the same limitation which was inserted into claim 1 by the previous amendment;

Claim 17 has been amended to correct its dependency in view of the cancellation of claim 16; and

Claim 19 has been amended to improve its readability without any change in the scope of the claim.

These additional amendments are enterable after Final as they do not raise new issues for examination and put the claims in better condition for allowance or appeal. Entry is therefore respectfully requested.

§103 Issues

Claims 1-6, 8, 13-16 and 19 have been rejected under 35 U.S.C. §103 as being obvious over GALATIK et al. (Czechoslovak Patent No. 264,719). Claims 7 and 17 have been rejected under 35 U.S.C. §103 as being unpatentable over GALATIK et al. as applied to claims 1-6, 8, 13-16 and 19, further in view of Balazs (U.S. 4,141,973) and Shimizu et al. (U.S. 4,024,073). Claims 9-12 have been rejected under 35 U.S.C. §103 as being unpatentable over GALATIK et al. as applied to claims 1-6, 8, 13-16 and 19, further in view of Applicants' disclosure at page 10, lines 15-27 of the specification. Applicants respectfully request reconsideration of these rejections on the ground that the GALATIK et al reference has been misapplied as a matter of law.

In the Final Office Action the arguments and evidence previously submitted as to the scope of the GALATIK teachings are reviewed and found non-persuasive on the

ground that criticality has not been shown. The Final Action misconstrues the arguments and/or misapplies the law.

Galatik Does Not Make out a *Prima Facie* Case of Obviousness

The evidence provided in the Johns declaration is directed to ascertaining what cross-link densities are provided at the extreme of the mole ratio range discussed in the GALATIK reference for the entire molecular weight range (and the slightly narrower enabled molecular weight range). This calculation exceeds the actual teachings which those skilled in the art would glean from the GALATIK reference. Most variables in chemical compositions are not completely independent. As a result, skilled persons expect that operating at the extreme of one variable will require optimization or near optimization of some or all other variables in the system. That is, they do not consider extremes of any range taught in a patent reference to be operative over the full range of any second variable. Therefore the Johns Declaration calculations, which look at the extremes of the mole ratio teachings over the full molecular weight range of the GALATIK hyaluronic acid teaching, define an area of crosslink-density which **exceeds** the actual teachings and suggestions provided by the reference to the skilled person. Because of this, a claim defining a crosslinked product whose crosslink density is outside the boundaries calculated by Dr. Johns cannot be argued to be *prima facie* obvious from GALATIK.

The upper boundary of crosslink density calculated by Dr. Johns, for a trivalent cation using the GALATIK mole ratios over the full MW range of 300,000-8,000,000 is represented graphically on the accompanying Exhibit A, together with the

boundary defined in independent claims 1 and 19. **There is no overlap.** The secondary references relied upon to reject claims 7 and 17 and 9-12, do nothing to create a suggestion or motivation to create a formulation which would exceed, expressly or inherently, the crosslink density boundary found by Dr. Johns' calculations. Because of this there is no *prima facie* obviousness from GALATIK.

Furthermore, GALATIK actually teaches away from the boundary conditions which Dr. Johns has found based solely on calculations directed to the extremes of the mole ratio and molecular weights defined by GALATIK. In particular, GALATIK teaches that "the effectiveness of drugs based on acid monosaccharides is ordinarily directly proportional to their specific molecular weight" (translation page 2). The crosslink density necessary to satisfy this motivation to crosslink is far less than the maximum crosslink density which results from the calculations of Dr. Johns. It is basic polymer chemistry that for a network polymer, the number of molecules in the system, regardless of mass, is unity, so that its molecular weight is infinite. In the case of the present crosslinked polymer system, just slightly more than two crosslinks per molecule produces a network. Additional crosslinks produce a tighter, more rigid molecule, but do not affect the molecular weight. Thus while the references to "dimers, trimers or higher order complexes" at page 3, first full paragraph, of the GALATIK translation may be read as teaching that three or even more crosslinks per molecule may be employed, and the ranges of the GALATIK claim allow for a much higher level than that, the motivation for crosslinking has already been maximized at three crosslinks per hyaluronate polymer molecule. There is no motivation provided by the

reference to continue to increase the density of crosslinks up to 60%, which in the case of even the minimum molecular weight materials of GALATIK would be more than 350 crosslinks per molecule (and higher as the molecular weight is increased), when a network polymer results from less than 3 crosslinks per molecule.

Criticality Is Not Necessary for Patentability

The Final Office Action asserts that criticality is needed to justify limiting the claims of the present invention to the disclosed preferred range, citing *Hays v. Reynolds, Comr. Pats.*, 145 USPQ 665 (DCDC 1965) and *In re Bourdon,* 112 USPQ 323 (CCPA 1957) as support. These cases are not on point to the issue presented here.

In *Hays*, a claim directed to a composition was held unpatentable on the ground of obviousness-type double patenting in view of a claim (of a commonly owned patent) which generically encompassed the subject matter of the claim at issue. Therefore a *prima facie* case of obviousness was made out by the prior claim. Criticality was needed in the *Hays* case to overcome the *prima facie* case. Here, unlike the *Hays v. Reynolds* case, it has been demonstrated that the **broadest** interpretations of the applicable prior art does not provide any overlap with the subject matter of the claims being presented. There is no *prima facie* case of obviousness here, and therefore there is no need for a showing of criticality.

In re Bourdon also involves a case in which the prior art was held to provide a general suggestion encompassing the range claimed. The case also appears to approve a rationale for rejection which has been expressly rejected in the case of *Andrew Corp. v.*

Gabriel Electronics, Inc., 6 USPQ2d 2010 (CAFC 1988). In the *Andrews* case the Federal Circuit stated at 6 USPQ2d 2014:

> Patentability is not measured against the closest point on the road to invention. Much technological change that meets the criterion of unobviousness, when viewed in light of the prior art, has a fuzzy boundary at its point of origin. Technological differences from prior art usually become more pronounced with distance from the boundary, but the changes may become manifest gradually. Indeed, the location of the boundary may well change with the available precision of measurement.
>
> *It is the prior public knowledge -- the "prior art" -- by which patentability is tested. A patentee may set the metes and bounds of that which is sought to be patented, and it is not material whether the phenomena just outside these claim limits are qualitatively different from that which is claimed.* The patentee is not required to show that some technological discontinuity exists between the claimed invention and the subject matter just outside the claims, but only that the claimed subject matter would have been nonobvious in view of the prior art. (*emphasis added*)

Thus the dicta of the *Bourdon* case can not be relied upon to justify a requirement for insisting on showing a showing of criticality for a range which is not itself suggested by the prior art.

Finally, the rejection is traversed because, while the improvement is manifested gradually, there is no question that the application evidences that the use of hyaluronate composition with crosslinking densities within the claimed range provides improved efficacy relative to that of compositions outside of the claimed range. See Example 5 and Tables 4-6 in the specification. This is result is unexpected and surprising from GALATIK whose teachings as a whole would lead to an expectation of optimal efficacy well below the maximum limitations taught in that reference.

GALATIK has been erroneously applied in all of the rejections under 35 USC §103. As noted above the secondary references do not affect the errors in application of the GALATIK reference and therefore all the §103 rejections are defective for the reasons just described. Accordingly withdrawal of all of the rejections under 35 USC §103 is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, the application is now believed to be in condition for allowance. Early and favorable action thereon is requested.

Respectfully submitted,

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Dated: February 2, 1996

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